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Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Jean Gosselin *et al.*

SERIAL NO.: 09/631,637 GROUP ART UNIT: 1648

FILED: August 2, 2000 EXAMINER: Ulrike Winkler

FOR: METHOD TO TREAT INFECTIOUS DISEASES AND/OR TO ENHANCE ANTIMICROBIAL EFFICACY OF DRUGS

REQUEST FOR PERSONAL INTERVIEW AND RECONSIDERATION

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

A Request for Continued Examination and a Petition for a three-month extension of time are being filed concurrently herewith.

REQUEST FOR PERSONAL INTERVIEW

Applicants believe that examination of the instant application can best be advanced by a direct discussion with the Examiner at which they could clarify various points relating to the application. Accordingly, they hereby respectfully request that their personal representatives be accorded an opportunity to meet with the Examiner before further action is taken on this case. Should the Examiner receive this filing before she has been contacted by applicants regarding the scheduling of such an interview, she is respectfully requested to contact the undersigned by telephone at (202) 624-2845.

REQUEST FOR RECONSIDERATION

Claims 1-3, 5-10 and 16-19 are pending. Claims 11-15 and 20-56 have been withdrawn from consideration by the Examiner.

Rejection under 35 U.S.C. § 112, first paragraph

The rejection of claims 1-3, 5-10 and 16-19 under 35 U.S.C. § 112, first paragraph, is respectfully traversed, and reconsideration and withdrawal are respectfully requested.

Although it is true that many drugs that have shown efficacy in *in vitro* or *in vivo* animal models do not reach commercialization and never end up on the pharmacy shelves, a demonstration of commercial practicability is not required to satisfy the requirements of § 112, first paragraph. See, *inter alia*, In re Brana, 34 USPQ2d 1346 (Fed. Cir. 1995). In many instances, the failure to reach commercialization is attributable not to lack of a desirable pharmacological activity, but to other factors, such as high toxicities, low bioavailability, too short half-life and too costly to manufacture. The Examiner cites one paper (Mitsuya et al., Science 226 : 172-174, 1984) on the *in vitro* anti-HIV effectiveness of suramin. Interestingly, despite nice *in vitro* anti-HIV effects, Mitsuya et al. caution the reader on the significant toxicities associated with suramin and that the use in humans should be monitored very closely. The Examiner subsequently refers to another paper by Sandström et al (Lancet, vol 1 pp 1480-82) and indicates that this paper teaches that *in vivo* experiments demonstrate no significant clinical or immunological improvement and the net effect of suramin was harmful. Based on this single example, the Examiner asserts that applicants *in vitro* tests are no indicator of *in vivo* activity.

Applicants have read the paper by Sandström and they could not find any statement to the effect that suramin does not cause clinical or

immunological improvement. The only sentence referring to suramin points out to the fact that suramin is even more toxic than PFA, a pyrophosphate analogue whose use is very limited as a consequence of its renal toxicities. Thus, it appears clear to the Applicants that suramin is not used in humans as a consequence of its high toxicity profile rather that to its lack of anti-HIV activity.

In vitro and animal experimentation represent the first in a long series of steps needed before a drug makes it on the market.

Since the filing of the above-captioned application, Applicants have conducted further experiments, namely they have obtained *in vivo* data supporting the anti-HIV activity of bpV (see previously submitted Exhibit 1). Briefly, using SCID mice reconstituted with human peripheral blood cells, Applicants clearly show (Figure 9) that bpV can effectively prevent the loss of CD4+ cells following HIV infection, results which are consistent with HIV inhibition. These results are therefore in complete agreement with results presented in Figures 1-8 of the instant patent application. Thus, the record does reflect *in vivo* activity.

Regarding the comments made in reference to the paper by Barbeau et al., (Journal of Biological Chemistry, 1997, 12968-12977), it is true that the results presented in figures 8 and 9, demonstrate HIV replication following bpV treatment. In the Barbeau paper, the authors report (figs. 8 and 9) that bpV induces the replication of HIV in the J1.1 and U1 cell lines. Importantly, these cell lines are latently infected with HIV, and therefore the virus is already integrated within the cell chromosome. The bpV activates the LTR promoter leading to increased proviral transcription and replication as reported under figures 8 and 9.

In sharp contrast to the experiments performed by Barbeau, the cell lines and primary cells used in the present application were not latently infected with HIV prior to bpV treatment. It is therefore very likely that bpV treatment alters HIV infection at a step prior to its integration. This would result in less cells being infected, leading to a reduction in viral production.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #2097/49123).

Respectfully submitted,

Date: May 13, 2003

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